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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,993	03/05/2002	Axel Ullrich	038602-1328	4467

22428 7590 12/16/2004

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EXAMINER	
ROBINSON, HOPE A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/087,993	ULLRICH ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-17 and 21-25* is/are pending in the application.

4a) Of the above claim(s) *13-17 and 21-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 March 2002 & 26 August 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/5/02*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *6/30/04*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. The Preliminary Amendments filed on March 5, 2002, July 1, 2002 and August 2, 2004 have been received and entered.

2. The Amendment filed on August 26, 2004 has been received, however, was not entered because the amendment is non-compliant. Amendments appear without underlining or brackets. See for example page 4 of the amendment, the paragraph replacement for page 13, line 35, has text that is not presently in the application and is not underlined and text is deleted without brackets. Also on page 6 of the amendment in the paragraph replacement for page 21, line 26, text from page 22 is missing and there is no indication that the text is to be deleted, and text from page 23 is inserted and there is no indication to insert that text.

Note that page 10 of the amendment has a replacement paragraph for page 69, line 31 which disclose the following sentence, "The PCT-2 nucleotide sequence (5581 bp) (SEQ ID NO:33) and deduced amino acid sequence (1430 amino acid) (SEQ ID NO:43) were determined", however, there are only 41 sequences in the application based on the sequence listing. Note also the typographical errors that appear on page 4 (see "deltion" and "resideues") and page 5 (see "trimester"). In addition, the amendments to the specification on page 69, line 31 has improper sequence notations, see "SEQ ID NOS 5, 39, 40 & 41 and SEQ ID NOS 37 & 38" and there is no colon in the notation, the proper sequence notation is "SEQ ID NO:". See page 10 of the amendment.

Claim Disposition

3. Claims 1-8, 18-20 and 26-27 have been canceled. Claims 11, 14 and 16 have been amended. Claims 9-17 and 21-25 are pending. Claims 9-12 are under examination.

4. In view of the Petition filed August 29, 2002, the inventorship in this nonprovisional application has been changed by the deletion of inventor Naohito Aoki, Hong Yang Wang, Shengjun Chen, Oliver Naylor and Alexei Kharitonenkov. The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

Specification

5. The specification is objected to because of the following informalities:

(a) The specification is objected to because on page 5, line 18, the following typographical error appears, "buman brain cDNA library", instead of "human brain cDNA library".

(b) The specification is objected to because on page 5, line 22 and page 73, line 26, it is disclosed that BDP-1 has 459 amino acids, however, the sequence listing provides 458 amino acid residues, see SEQ ID NO:36.

(c) The specification is objected to because trademarks are disclosed throughout the instant specification and not all of them are capitalized or accompanied by the generic terminology. The use of the trademark such as TRITON™, for example, has been noted in this application (see page 92). It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the

proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

(d) The specification is objected to because the amendment to specification filed on March 5, 2002 instructs the PTO to insert a paragraph, which does not include the provisional applications in the continuity data. It is suggested that page 1 of the instant specification is amended to disclose the following priority information: "This application is a continuation of U.S. Application No. 08/877,150, filed June 17, 1997, which claims benefit of Provisional Applications 60/023,485, filed August 9, 1996; 60/030,860, filed November 13, 1996; 60/030,964, filed November 15, 1996; 60/034,286, filed December 19, 1996 and 60/019,629, filed June 17 1996.

(e) On page 79, line 18, the following typographical error appears "pancreasee" which should be "pancreas".

(f) The specification is objected to because the amendments made on August 2, 2004, have improper sequence notations, see for example page 2, FIG 2a-f, "SEQ ID NOS 33 and 34 respectively", which should be "SEQ ID NOS: 33 and 34 respectively". See also page 3 of the amendment filed on August 2, 2004.

Correction of the above and compliance with the sequence rules is required.

Information Disclosure Statement

6. The information disclosure statement filed on March 5, 2002 is acknowledged. The references cited on the PTO-1449 Form have been considered by the examiner and copies of the

PTO-1449 Form are attached to the instant Office action. Note however, that item "AD" has been lined through because the citation is incomplete, no date is provided for the citation.

Correction is required.

Drawing

7. The drawings filed on March 5, 2002 are objected to because of inconsistencies, for example, the sequences presented in Figures 2 and 3 when read from top to bottom do not correspond with the sequence listing. It is noted that the Amendment filed on August 2, 2004 indicates that "as diagrammed on page 3/15 of the figures, figure 3a should be viewed adjacent to figure 3b and figure 3c should be viewed adjacent to figure 3d. It is suggested that the Figures are amended to read from top to bottom as recognized in the prior art. Further Figures 2 and 3 on page 3 are not figures *per se* thus should be deleted. Further, several inconsistencies exist within the sequences disclosed as Figures 2-3, for example Figure 3a has the residue H listed for the codon TGG which should be residue W and other errors are pointed on in the remarks filed on August 2, 2004 (see pages 5-11). The remarks filed on August 2, 2004 indicate that typographical errors occurred and provided the correct residues to match the codons, however, note that Figure 2e has the codon CGT (at base number 1077) listed as G and has been corrected as H, however that codon does not code for G or H, instead codes for R. Thus, it is unclear if the DNA or the amino acid sequence is incorrect. It is noted that applicant filed corrected drawings on August 26, 2004, which corrects most of the inconsistencies discussed above. However, the amendments to the drawings have not been entered as amendments made concurrently to the instant specification were not entered and affects entry of the drawing amendments. It is also

noted that applicant's Figure 1 is a schematic of Figures 2a-2d, it is suggested that applicant present the sequence to be read from top to bottom with continuing pages, and delete the schematic which does not represent a figure *per se*.

Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 9-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a BDP1 (brain derived protein) polypeptide, however, the claims have no structural limitation as the claims do not recite a specific sequence, nor any functional limitation (see claims 9-10). It is noted that claim 11 provides a structure to rectify the deficiency of claims 9-10, however the claim is directed to a polypeptide comprising at least 12 contiguous amino acids from SEQ ID NO:36 and there is no functional limitation to indicate that the recited fragment would be biologically active or retain the function that the full length sequence possesses. Thus, the claims encompass a genus of polypeptides that are not adequately described. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice,

reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species that are adequately described are representative of the entire genus.

The specification on page 5 indicates that the BDP1 polypeptide shares 85% sequence homology to PTP20 and shares 36 to 38%% homology with the PTPase-PEST family. It is further disclosed that BDP1 has tyrosine phosphatase activity (see page 6). However, the instant specification does not demonstrate possession of the genus of polypeptide encompassed in the claims or provide any evidence that said genus has the tyrosine phosphatase activity. As the proteins vary in structure, they function differently. One of skill in the art needs to know when one is in possession of the claimed invention, thus the claims should recite the structure and function of the claimed protein.

Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991), states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity

or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993).* Therefore, for all these reasons adequate written description is lacking, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

9. Claims 9-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the proteins set forth in SEQ ID NO: 36, does not reasonably provide enablement for all the possible fragments encompassed in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The enablement requirement refers to the requirement that the specification describe how to make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims (see *In re Wands, 858 F.2d at 737, 8 USPQ2d at1404 (Fed. Cir. 1988*). The factors most relevant to the instant invention are discussed below.

Breath of claims: The claims are overly broad in scope as claims such as 10 and 11 encompass an unspecified amount of fragments of the claimed polypeptide as long as the fragment is "unique" and comprises at least 12 contiguous amino acids. The scope of the claims encompass any fragment having any function, including non-functional polypeptides and polypeptides having function other than a tyrosine phosphatase activity. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides having any function as broadly encompassed by the claims. The application is limited to the polypeptide set forth in SEQ ID NO:36.

The lack of guidance and working examples: The claims are directed to a single sequence (SEQ ID NO:36) and the instant specification does not provide examples that are commensurate in scope with the claims which encompass an unspecified amount of variants. The recited SEQ ID NO:36 is insufficient to provide the necessary guidance for making and/or using the entire scope of the claimed polypeptides, which encompass variants and fragments. A skilled artisan recognizes that such polypeptides have the potentiality of having any function or no function. The specification fails to provide guidance regarding those regions or fragments that are necessary for the tyrosine phosphatase activity, what regions are conserved and exemplify said fragments.

The high degree of unpredictability of the art: Predictability of which potential changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. One of

skill in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. In this case, the necessary guidance has not been provided in the specification. Thus, a skilled artisan would recognize the high degree of unpredictability that all polypeptides comprising as few as 12 amino acids would retain the tyrosine phosphatase activity.

The state of the prior art: The state of the prior art provides evidence for the high degree of unpredictability as stated above. Seffernick et al. (J. Bacteriology, volume 183, pages 2405-2410, 2001) disclose two polypeptides having 98% amino acid sequence identity and 99% sequence identity at the nucleic acid level, differing at only 9 out of 475 amino acids (page 2407, right column, middle and page 2408, Figure 3). The polypeptides of Seffernick et al. are identical along relatively long stretches of their respective sequences (page 2408, Figure 3), however, these polypeptides exhibit distinct functions. Thus, the positions within an encoding polynucleotide's sequence where nucleotide modifications can be made with a reasonable expectation of success in obtaining an encoded polypeptide with the desired activity are limited in any protein and the result of such modification for a given protein diminish with each further and additional modification.

The amount of experimentation required is undue: While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims. In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the state of the prior art, undue experimentation

would be necessary for a skilled artisan to make and use the entire scope of the claimed polypeptides.

The issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)*. Therefore, absent direction/guidance regarding whether the structure of the BDP1 polypeptide can tolerate the modifications contemplated a non-functional protein may result and one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims.

Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting to construct and test variants of the claimed invention would constitute undue experimentation. Making and testing the infinite number of possible fragments to find one that functions as described is undue experimentation. Therefore, applicants have not

provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

10. Claims 9-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is indefinite because the mere recitation of "BDP1" is insufficient to convey what applicant intends to be the claimed invention, the spelled out meaning of the acronym should be recited in the claim (Brain Derived Phosphatase) because the acronym could represent the tri-peptide, for example, "Asx-Asp-Pro" (Asparagine-Aspartic acid-Proline). Additionally, the claim recites an isolated, purified, or enriched BDP1 polypeptide, which is a compound and "enriched" addresses concentration, thus a composition, thus it is unclear how the above compound is enriched. It is noted that page 11 of the instant specification defines the term "enriched" in reference to the nucleic acid, however, no definition is provided for the polypeptide. It is suggested that the term "enriched" is deleted from the claim as there is no standard for ascertaining the requisite degree and the term is usually associated with a composition, not a compound *per se*. The dependent claims hereto are also included in this rejection.

Art* of *Record

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Kim et al. (Oncogene, vol. 13, 1996, cited on PTO-1449). Kim et al. teach the PEST family protein tyrosine phosphatase BDP1. However, Kim et al. is not considered to be a prior art reference based on the date of publication.

Conclusion

12. No claims are presently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS
12/10/04

Patent Examiner